RAW SEQUENCE LISTING

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) no errors detected.

Application Serial Number: 10/658,355C
Source: IFW16
Date Processed by STIC: 11/15/2006

ENTERED

IFW16

RAW SEQUENCE LISTING DATE: 11/15/2006
PATENT APPLICATION: US/10/658,355C TIME: 11:44:02

Input Set : F:\923SEQ.004.txt
Output Set: N:\CRF4\11152006\J658355C.raw

<110> APPLICANT: Gantier, Rene
Guyon, Thierry
Hugo, Cruz Ramos
Vega, Manuel
Drittanti, Lila
<120> TITLE OF INVENTION: Rational Directed Protein Evolution Using Two Dimensional Rational Mutagenesis Scanning
<130> FILE REFERENCE: 17019-013001/923
<140> CURRENT APPLICATION NUMBER: US/10/658,355C
<141> CURRENT FILING DATE: 2003-09-08
<150> PRIOR APPLICATION NUMBER: 60/457,063
<151> PRIOR FILING DATE: 2003-03-21
<150> PRIOR APPLICATION NUMBER: 60/410,258
<151> PRIOR FILING DATE: 2002-09-09
<160> NUMBER OF SEQ ID NOS: 502
<170> SOFTWARE: FastSEQ for Windows Version 4.0
<210> SEQ ID NO: 1
<211> LENGTH: 165
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<400> SEQUENCE: 1

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
        35                  40                  45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
    50                  55                  60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65                  70                  75                  80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
                85                  90                  95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
            100                 105                 110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
        115                 120                 125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
    130                 135                 140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145                 150                 155                 160
Leu Arg Ser Lys Glu
                165
```

RAW SEQUENCE LISTING DATE: 11/15/2006
PATENT APPLICATION: US/10/658,355C TIME: 11:44:02

Input Set : F:\923SEQ.004.txt
Output Set: N:\CRF4\11152006\J658355C.raw

<210> SEQ ID NO: 2
<211> LENGTH: 165
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: D2A Mutant INF-alpha 2b
<400> SEQUENCE: 2

```
Cys Ala Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
        35                  40                  45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
    50                  55                  60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65                  70                  75                  80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
                85                  90                  95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
            100                 105                 110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
        115                 120                 125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
    130                 135                 140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145                 150                 155                 160
Leu Arg Ser Lys Glu
                165
```

<210> SEQ ID NO: 3
<211> LENGTH: 165
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: P4A Mutant INF-alpha 2b
<400> SEQUENCE: 3

```
Cys Asp Leu Ala Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
        35                  40                  45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
    50                  55                  60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65                  70                  75                  80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
                85                  90                  95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
```

RAW SEQUENCE LISTING DATE: 11/15/2006
PATENT APPLICATION: US/10/658,355C TIME: 11:44:02

Input Set : F:\923SEQ.004.txt
Output Set: N:\CRF4\11152006\J658355C.raw

```
133             100                 105                 110
135 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
136         115                 120                 125
138 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
139     130                 135                 140
141 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
142 145                 150                 155                 160
143 Leu Arg Ser Lys Glu
144                 165
146 <210> SEQ ID NO: 4
147 <211> LENGTH: 165
148 <212> TYPE: PRT
149 <213> ORGANISM: Artificial Sequence
151 <220> FEATURE:
152 <223> OTHER INFORMATION: Q5A Mutant INF-alpha 2b
154 <400> SEQUENCE: 4
155 Cys Asp Leu Pro Ala Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
156  1               5                  10                  15
158 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
159             20                  25                  30
161 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
162         35                  40                  45
164 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
165     50                  55                  60
167 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
168 65                  70                  75                  80
170 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
171                 85                  90                  95
173 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
174             100                 105                 110
176 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
177         115                 120                 125
179 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
180     130                 135                 140
182 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
183 145                 150                 155                 160
184 Leu Arg Ser Lys Glu
185                 165
187 <210> SEQ ID NO: 5
188 <211> LENGTH: 165
189 <212> TYPE: PRT
190 <213> ORGANISM: Artificial Sequence
192 <220> FEATURE:
193 <223> OTHER INFORMATION: T6A Mutant INF-alpha 2b
195 <400> SEQUENCE: 5
196 Cys Asp Leu Pro Gln Ala His Ser Leu Gly Ser Arg Arg Thr Leu Met
197  1               5                  10                  15
199 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
200             20                  25                  30
```

RAW SEQUENCE LISTING DATE: 11/15/2006
PATENT APPLICATION: US/10/658,355C TIME: 11:44:02

Input Set : F:\923SEQ.004.txt
Output Set: N:\CRF4\11152006\J658355C.raw

```
202 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
203         35                  40                  45
205 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
206     50                  55                  60
208 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
209 65                  70                  75                  80
211 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
212                 85                  90                  95
214 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
215             100                 105                 110
217 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
218         115                 120                 125
220 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
221     130                 135                 140
223 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
224 145                 150                 155                 160
225 Leu Arg Ser Lys Glu
226                 165
228 <210> SEQ ID NO: 6
229 <211> LENGTH: 165
230 <212> TYPE: PRT
231 <213> ORGANISM: Artificial Sequence
233 <220> FEATURE:
234 <223> OTHER INFORMATION: H7A Mutant INF-alpha 2b
236 <400> SEQUENCE: 6
237 Cys Asp Leu Pro Gln Thr Ala Ser Leu Gly Ser Arg Arg Thr Leu Met
238  1               5                  10                  15
240 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
241             20                  25                  30
243 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
244         35                  40                  45
246 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
247     50                  55                  60
249 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
250 65                  70                  75                  80
252 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
253                 85                  90                  95
255 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
256             100                 105                 110
258 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
259         115                 120                 125
261 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
262     130                 135                 140
264 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
265 145                 150                 155                 160
266 Leu Arg Ser Lys Glu
267                 165
269 <210> SEQ ID NO: 7
270 <211> LENGTH: 165
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RAW SEQUENCE LISTING DATE: 11/15/2006
PATENT APPLICATION: US/10/658,355C TIME: 11:44:02

Input Set : F:\923SEQ.004.txt
Output Set: N:\CRF4\11152006\J658355C.raw

<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: S8A Mutant INF-alpha 2b
<400> SEQUENCE: 7

```
Cys Asp Leu Pro Gln Thr His Ala Leu Gly Ser Arg Arg Thr Leu Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
        35                  40                  45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
    50                  55                  60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65                  70                  75                  80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
                85                  90                  95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
            100                 105                 110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
        115                 120                 125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
    130                 135                 140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145                 150                 155                 160
Leu Arg Ser Lys Glu
                165
```

<210> SEQ ID NO: 8
<211> LENGTH: 165
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: L9A Mutant INF-alpha 2b
<400> SEQUENCE: 8

```
Cys Asp Leu Pro Gln Thr His Ser Ala Gly Ser Arg Arg Thr Leu Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
        35                  40                  45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
    50                  55                  60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65                  70                  75                  80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
                85                  90                  95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
            100                 105                 110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
```

RAW SEQUENCE LISTING ERROR SUMMARY DATE: 11/15/2006
PATENT APPLICATION: **US/10/658,355C** TIME: 11:44:03

Input Set : **F:\923SEQ.004.txt**
Output Set: **N:\CRF4\11152006\J658355C.raw**

Please Note:
Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:195; N Pos. 1,22

VERIFICATION SUMMARY DATE: 11/15/2006
PATENT APPLICATION: **US/10/658,355C** TIME: 11:44:03

Input Set : **F:\923SEQ.004.txt**
Output Set: **N:\CRF4\11152006\J658355C.raw**

L:7601 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:195 after pos.:0